THE DIAGNOSIS OF CHOLECYSTIC DISEASE*

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THIS subject is best approached by beginning with a study of the formation of bile and observing it through its normal passage to the intestinal tract.

The bile as it leaves the liver contains less than 5 per cent of solid matter; the rest is water. The solid matter contains bile salts, bile pigment, nucleo-protein and cholesterol; other solids of less importance are lecithin, inorganic salts, and fat. The bile salts are the only solids secreted by liver cells; others pass through the liver and are excreted unchanged. During the periods when digestion is actively taking place the bile flows in a continuous stream from the liver cells through the biliary channels into the duodenum. During the fasting periods its entrance into the duodenum is effectively blocked by the closure of the sphincter of Oddi, which remains tonically contracted. The pressure in the bile ducts rises as bile accumulates within the ducts and finally forces its way through the cystic duct into the gall bladder. After the bile reaches the gall bladder it undergoes certain changes. Rapid concentration takes place, water and organic salts are absorbed by the lymphatics in the gall-bladder wall, and the specific gravity of the gall-bladder bile is raised. Cholesterol is not absorbed, neither are the bile salts, and the bile which remains in the gall bladder becomes much thickened and is often ten times as concentrated as liver bile. The fluid which is absorbed is practically the same as normal saline. Not only does the bile become concentrated in the gall bladder but it becomes acid and is mixed with a mucous secretion contributed by the bladder wall, which adds viscosity to its other qualities. Thus we see that gall-bladder bile differs greatly from liver bile.

The constituent elements of gall stones are found to be the solids contained in bile, and although the mechanism of gall-stone formation is not exactly understood it seems to be closely connected with or dependent upon gall-bladder dysfunction. Several types of calculi are possible, and it seems reasonable to assume that there may be several factors which play a part in the formation of gall stones. The large single stone which is almost pure cholesterol, the mixed cholesterin stone which is found in a large variety of both sizes and numbers, and the mixed bilirubin calcium stones which only occur in small numbers, are not likely to have the same etiological background. Bile stasis, disturbances of metabolism, and infection may all play a part in causing whatever disturbance is necessary to throw the solid constituents of the bile out of solution, resulting in calculus formation. The nucleus is commonly pure or almost pure cholesterol. That calculi may form silently and be unaccompanied by symptoms seems certain, as many patients carry them about for years without any noteworthy symptoms. Once the gall bladder, laden with stones, becomes infected and the element of inflammation is added, we have a patient who may present a wide variation in findings and a great variety of symptoms.

Infection reaches the gall bladder in two ways: (1) by way of the bile stream; (2) by way of the systemic circulation.

Bacteria are constantly transmitted from the intestinal tract through the portal circulation to the liver, which is endowed with antibacterial as well as antitoxic properties. Under normal conditions the bacteria received in this way are destroyed and the bile leaving the liver is sterile. But if the virulence of the bacteria is high, or the destructive power of the liver be lessened, the bacteria are not destroyed but are excreted in the bile and enter the gall bladder by way of the biliary ducts. If the mucous lining of the gall bladder has been injured or irritated by calculi some degree of cholecystitis may result. Streptococcus, *B. coli*, staphylococcus, *Cl. Welchii* and *B. typhosus* have all been isolated from gall-bladder bile or the gall-bladder wall by various observers. Once infected, the function of the gall bladder is interfered with and the wall loses its power to concentrate bile to some degree, and many chronically thickened gall bladders, the site of old long-standing inflammation, have ceased to function physiologi-

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cally. The diseased gall bladder containing calculi and infective agents may be the cause of degenerative pathological processes of a general character, and the symptoms and signs are not always localized to the region of the gall bladder.

Cholecystic disease is characterized by its chronicity, and it is doubtful if what the surgeon knows as acute cholecystitis ever exists, except as an acute exacerbation in a chronically diseased gall bladder. Because of its chronicity, as well as the combination of calculi and infection in most cases, the disease presents a wide variety of clinical symptoms. Symptoms are often very vague in character, and often very dramatic in their onset. The clinical picture, too, is modified by the fact that a certain degree of chronic hepatitis is always present and liver function therefore interfered with.

An analysis of 100 consecutive cases of gall-bladder disease where the gall bladder was removed has been made with a view to evaluating various symptoms and signs.

It is generally conceded that over half the cases of chronic dyspepsia are due to biliary tract disease, and we expect to find a history of indigestion in gall-stone sufferers. In this series 57 did not give a history of indigestion, and stated that they could eat anything before the onset of the present illness. Forty-three had an established intolerance to food of some sort. Six could not take any food without distress following. Twenty-two could not tolerate fats, and 12 could not tolerate meat of any sort. Other articles of diet were recorded as objectionable in a few cases. When dyspepsia was an established factor the patient's complaints were usually fullness in the epigastrium, flatulent distension, eructations or frequent biliary colics. Rich fatty foods were usually found to increase these symptoms. Seventeen recorded constipation, and 6, diarrhœa. The recent attack was associated with nausea and vomiting in 64 cases, and nausea alone in 13 others.

The most prominent and constant symptom complained of in these cases was pain. Eighty-eight had pain recorded as the chief complaint on admission. Forty-eight had pain in the right upper quadrant; 32 in the epigastrium; 6 on the right half of the abdomen; and 2 in the left upper quadrant. The character of the pain in biliary tract disease is likely to vary considerably, and various terms may be used by the patient in describing it; dull, crampy, sharp, colicky, agonizing, stabbing, steady, are terms that have been given to us by patients in describing their pain. As pain is a relative term, one must concede to the patient the privilege of giving his own description of it. The pain of a typical biliary colic comes on suddenly, with cramps in the epigastrium which double up the patient. Often he is deathly pale and is covered with cold sweat. The pain will be *referred* in a great many instances. In 37 it was referred to the shoulder, in 22 to the back, and in 4 to both shoulders. A close analysis of the pain is of value. Only a few gave a history of a definite colic; in most the pain was constant, dull and agonizing. If an established chronic pain is epigastric rather than limited to the right side it is usually due to peri-cholecystic adhesions, and, if so, is likely to be increased after meals. Where peri-cholecystic adhesions mask the picture the pain may closely simulate the pain of duodenal ulcer, and a barium meal with an x-ray of the stomach and duodenum may be necessary to clear up the diagnosis. It must be kept in mind that both conditions may be present in the same patient. Duodenal ulcer was present as a complicating disease in 4 of this series. Pain involving the right half of the abdomen indicates that inflammation in the appendix is likely to be active. Chronic appendicitis was found associated with gall-bladder disease in 36 of the 73 patients who still had their appendices.

The presence or absence of jaundice in the gall-bladder patient should always be noted, and the history of previous attacks checked. Twenty-one patients were jaundiced on admission. The degree of jaundice is important, and is best estimated by the icterus index and van den Bergh tests. Patients who have no visible jaundice may have a high bilirubinæmia, as neither skin nor sclera will show a yellow tint until the icterus index reaches 15 by the Bernheim colorimeter. Therefore, the recording of the icterus index and van den Bergh readings should be done as a routine. Acholic stools and highly coloured urine will both be accompanied by an increase in the blood bilirubin. The most satisfactory way of estimating the degree of jaundice is by the recording from day to day of the icterus index. Day to day estimates should be made as operation is con-

traindicated when the serum pigment curve is on the ascent.

Not all jaundiced patients have gall stones or even cholecystitis. Jaundice may be obstructive, intra-hepatic or hæmolytic. Obstructive jaundice is due to mechanical blocking of the bile ducts, which results in absorption of bile pigment. Intra-hepatic jaundice is due to infection and the parenchymal liver cells are unable to excrete the bile pigment in the normal manner. In hæmolytic jaundice there is an excessive destruction of red cells so that bilirubin forms more rapidly than normal and is retained in the blood stream. The van den Bergh test assists in differentiating between obstructive and non-obstructive jaundice. We get what is called a *direct* reaction in the obstructive type, and only get a reaction after the *indirect* method is employed in non-obstructive jaundice. When obstructive jaundice is due to a stone in the common duct the nature of the jaundice may vary considerably. It may be temporary, intermittent, or continuous. Intermittent jaundice usually means the passage of several stones at intervals, or a stone lodged in the ampulla of Vater which acts as a ball valve. Long-continued jaundice usually indicates cholangitis or an impacted stone.

In cases where the jaundice is due to carcinoma of the head of the pancreas the jaundice has likely come on insidiously and without any history of pain. It is often stated that pancreatic jaundice never produces itching skin, but this is not so. Pancreatic jaundice may produce itching the same as liver jaundice.

Jaundiced patients bleed readily and the clotting time is likely to be several times the length of normal. For this reason the clotting time should be estimated, and, where possible, any operation preceded by a blood transfusion and the administration of calcium gluconate.

In most cases the history, with an analysis of the pain and the physical findings, will give sufficient data on which to make a diagnosis, but when there is still uncertainty two important clinical tests are still available, duodenal drainage and cholecystography. A diagnostic duodenal drainage was done on 16 cases in the series, and in 15 the test indicated a diseased gall bladder. When the gall-bladder bile contains pus and crystals it is taken to indicate gall-bladder disease. It was found advisable to obtain an x-ray of the gall bladder after the injection of iodeikon in 33 cases. Of these 22 had findings indicating disease, and 11 were negative. This is a poorer showing than is usually expected, but indicates that even if the radiologist's report is negative the gall bladder may still be diseased.

As 7 of this series had previously had cholecystostomies performed, an analysis of these seven was made to see if they presented any symptoms different from the others. One had had cholecystostomy done seven years previously, one, five years, and the others at shorter periods, ranging down to less than one year. Two still had a persisting biliary fistula, and the other 5 had visible jaundice on admission to hospital, and gave a history of pain in the region of the gall bladder and digestive disturbances. All 7 pathological reports showed chronic cholecystitis, and 4 cholelithiasis. In addition one had an adenocarcinoma commencing in the gall-bladder wall on the side distal to the liver. In all the diagnosis of a pathological gall bladder was apparent on admission to hospital.

Diagnosis can be definitely made in almost all cases of cholecystic disease if all the methods now at our disposal are utilized. Where doubt exists the clinical symptoms are likely to be mild and the patient can readily wait until diagnosis is certain. No gall bladder should be condemned without clinical evidence of disease.

THE DANGER OF EATING RHUBARB LEAVES.—Because rhubarb sauce and rhubarb pie are frequent articles in the American diet, the use of the leaf blades for greens has frequently been suggested. J. H. Beattie states that numerous cases of more or less serious illness and some fatalities have been reported in Europe and North America from the use of rhubarb leaves. The rhubarb leaf blades were eaten boiled in the belief that they were substitutes for the common greens. A fatal case of poisoning following the ingestion of rhubarb leaves was reported in the Journal, August 23, 1919, page 627, while additional correspondence appeared in the issues of September 20 and October 11, 1919. Beattie states that "owing to the high content of oxalic acid and its soluble salts found in rhubarb leaves it is recommended that they be left entireley alone and not used under any circumstances as food. In the stalks, however, the oxalic acid is present in smaller amount and largely in insoluble form, and for this reason is harmless."—*J. Am. M. Ass.*, 1937, **109**: 960.